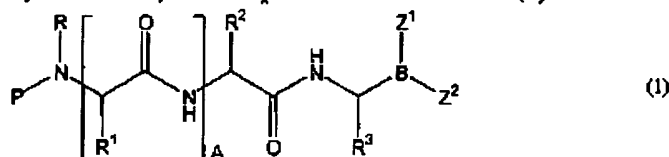


In re Appln. of Shanker GUPTA
Application No. 10/056,567

CLAIM AMENDMENTS

1. (Currently Amended) A compound of the formula (1):



wherein

P is hydrogen or an amino-group protecting moiety;

R is hydrogen or alkyl;

A is 0, 1, or 2;

R¹, R², and R³ are each independently hydrogen, alkyl, cycloalkyl, aryl, or -CH₂-R⁵;

R⁵, in each instance, is aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, heteroaryl, or -W-R⁶, where W is a chalcogen and R⁶ is alkyl;

wherein the ring portion of any said aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, or heteroaryl in R¹, R², R³, or R⁵ can be optionally substituted; and

Z¹ and Z² together form a moiety derived from a sugar, wherein the atom attached to boron in each case is an oxygen atom, and wherein the sugar is mannitol.

2. - 4. (Canceled)

5. (Original) The compound of claim 1, wherein A is 0.

6. - 7. (Canceled)

8. (Original) The compound of claim 1, wherein P is R⁷-C(O)-, R⁷-S(O)₂-, R⁷-NH-C(O)-, or R⁷-O-C(O)-;

where R⁷ is alkyl, aryl, alkaryl, or aralkyl, any of which can be optionally substituted, or when P is R⁷-C(O)- or R⁷-S(O)₂-, R⁷ can also be an optionally substituted 5- to 10-membered saturated, partially saturated, or aromatic heterocycle.

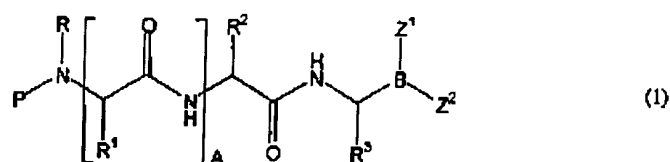
9. (Original) The compound of claim 8, wherein P is R⁷-C(O)- or R⁷-S(O)₂-, and R⁷ is an aromatic heterocycle.

10. (Original) The compound of claim 9, wherein P is (2-pyrazine)carbonyl or (2-pyrazine)sulfonyl.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

11. (Original) The compound of claim 8, wherein
A is zero;
R is hydrogen or C₁-C₈ alkyl; and
R³ is C₁-C₆ alkyl.
12. (Currently Amended) The compound of claim 11, wherein P is (2-pyrazine)carbonyl or (2-pyrazine)sulfonyl.
13. (Canceled)
14. (Original) The compound of claim 1, wherein
R¹, R², and R³ are each independently hydrogen, C₁-C₈ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₀ aryl, or -CH₂-R⁵;
R⁵ in each instance is C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆)alk(C₆-C₁₀)aryl, C₃-C₁₀ cycloalkyl, C₁-C₈ alkoxy, or C₁-C₈ alkylthio;
wherein the ring portion of any said aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, or heteroaryl groups of R¹, R², R³, or R⁵ can be optionally substituted.
15. (Original) The compound of claim 1, wherein said compound is:
D-Mannitol *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate;
D-Mannitol *N*-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronate;
D-Mannitol *N*-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronate;
D-Mannitol *N*-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronate;
D-Mannitol *N*-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronate;
D-Mannitol *N*-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronate;
D-Mannitol *N*-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronate;
D-Mannitol *N*-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronate; or
D-Mannitol *N*-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronate.
16. (Original) The compound D-mannitol *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate.
17. (Currently Amended) A lyophilized compound of the formula (1):

In re Appln. of Shanker GUPTA
Application No. 10/056,567



wherein

P is hydrogen or an amino-group protecting moiety;

R is hydrogen or alkyl;

A is 0, 1, or 2;

R^1 , R^2 , and R^3 are each independently hydrogen, alkyl, cycloalkyl, aryl, or $-\text{CH}_2-\text{R}^4$;

R^5 , in each instance, is aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, heteroaryl, or $-\text{W}-\text{R}^6$, where W is a chalcogen and R^6 is alkyl;

wherein the ring portion of any said aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, or heteroaryl in R^1 , R^2 , R^3 , or R^5 can be optionally substituted; and

Z^1 and Z^2 together form a moiety derived from a sugar, wherein the atom attached to boron in each case ~~is~~ is an oxygen atom, and wherein the sugar is mannitol.

18. - 19. (Canceled)

20. (Original) The compound of claim 17, wherein A is 0.

21. - 23. (Canceled)

24. (Original) The compound of claim 17, wherein P is $\text{R}^7-\text{C}(\text{O})-$, $\text{R}^7-\text{S}(\text{O})_2-$, $\text{R}^7-\text{NH}-\text{C}(\text{O})-$, or $\text{R}^7-\text{O}-\text{C}(\text{O})-$;

where R^7 is alkyl, aryl, alkaryl, or aralkyl, any of which can be optionally substituted, or when P is $\text{R}^7-\text{C}(\text{O})-$ or $\text{R}^7-\text{S}(\text{O})_2-$, R^7 can also be an optionally substituted 5- to 10-membered saturated, partially saturated, or aromatic heterocycle.

25. (Original) The compound of claim 24, wherein P is $\text{R}^7-\text{C}(\text{O})-$ or $\text{R}^7-\text{S}(\text{O})_2-$, and R^7 is an aromatic heterocycle.

26. (Original) The compound of claim 25, wherein P is (2-pyrazine)carbonyl or (2-pyrazine)sulfonyl.

27. (Original) The compound of claim 24, wherein
A is zero;

In re Appln. of Shanker GUPTA
Application No. 10/056,567

R is hydrogen or C₁-C₈ alkyl; and
R³ is C₁-C₆ alkyl.

28. (Currently Amended) The compound of claim 27, wherein P is (2-pyrazine)carbonyl or (2-pyrazine)sulfonyl.

29. (Canceled)

30. (Original) The compound of claim 17, wherein

R¹, R², and R³ are each independently hydrogen, C₁-C₈ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₀ aryl, or -CH₂-R⁵;

R⁵ in each instance is C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆)alk(C₆-C₁₀)aryl, C₃-C₁₀ cycloalkyl, C₁-C₈ alkoxy, or C₁-C₈ alkylthio;
wherein the ring portion of any said aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, or heteroaryl groups of R¹, R², R³, or R⁵ can be optionally substituted.

31. (Original) The compound of claim 25, wherein said compound is:

D-Mannitol *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate;

D-Mannitol *N*-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronate;

D-Mannitol *N*-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronate;

D-Mannitol *N*-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronate;

D-Mannitol *N*-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronate;

D-Mannitol *N*-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronate;

D-Mannitol *N*-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronate;

D-Mannitol *N*-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronate; or

D-Mannitol *N*-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronate.

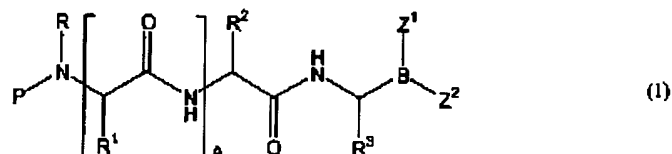
32. (Original) The lyophilized compound D-mannitol *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate.

33. (Original) The compound of claim 17, wherein the compound is stable at 0 °C for at least one month.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

34. (Original) The compound of claim 17, wherein the compound is stable at 40 °C for at least one month.

35. (Currently Amended) A method of preparing a lyophilized compound of the formula (1):



wherein

P is hydrogen or an amino-group protecting moiety;

R is hydrogen or alkyl;

A is 0, 1, or 2;

R¹, R², and R³ are each independently hydrogen, alkyl, cycloalkyl, aryl, or -CH₂-R⁵;

R⁵ in each instance is aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, heteroaryl, or -W-R⁶, where W is a chalcogen and R⁶ is alkyl;

wherein the ring portion of any said aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, or heteroaryl in R¹, R², R³, or R⁵ can be optionally substituted; and

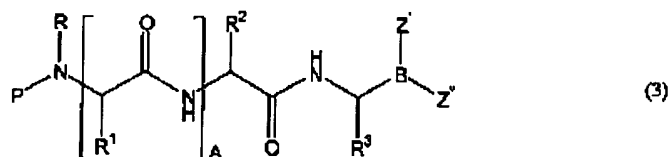
Z¹ and Z² together form a moiety derived from a sugar;

the method comprising:

(a) preparing a mixture comprising

(i) water,

(ii) a compound of formula (3).



wherein P, R, A, R¹, R², and R³ are as described above; and

Z' and Z'' are OH; and

(iii) ~~a-sugar~~ mannitol; and

(b) lyophilizing the mixture.

36. - 40. (Canceled)

In re Appln. of Shanker GUPTA
Application No. 10/056,567

41. (Original) The method of claim 35, wherein P is R^7 -C(O)-, R^7 -S(O)₂-, R^7 -NH-C(O)-, or R^7 -O-C(O)-;

where R^7 is alkyl, aryl, alkaryl, or aralkyl, any of which can be optionally substituted, or when P is R^7 -C(O)- or R^7 -S(O)₂-, R^7 can also be an optionally substituted 5- to 10-membered saturated, partially saturated, or aromatic heterocycle.

42. (Original) The method of claim 41, wherein P is R^7 -C(O)- or R^7 -S(O)₂-, and R^7 is an aromatic heterocycle.

43. (Original) The method of claim 42, wherein P is (2-pyrazine)carbonyl or (2-pyrazine)sulfonyl.

44. (Original) The method of claim 35, wherein

A is zero;

R is hydrogen or C₁-C₆ alkyl; and

R³ is C₁-C₆ alkyl.

45. (Currently Amended) The method of claim 44, wherein P is ~~(2-pyrazine)carbonyl or~~ (2-pyrazine)sulfonyl.

46. (Original) The method of claim 35, wherein

R¹, R², and R³ are each independently hydrogen, C₁-C₈ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₀ aryl, or -CH₂-R⁵;

R⁵ in each instance is C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆)alk(C₆-C₁₀)aryl, C₃-C₁₀ cycloalkyl, C₁-C₈ alkoxy, or C₁-C₈ alkylthio;

wherein the ring portion of any said aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl, or heteroaryl groups of R¹, R², R³, or R⁵ can be optionally substituted.

47. (Original) The method of claim 35, wherein the compound of formula (3) is:

N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid;

N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid;

N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid;

N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid;

N-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid;

N-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid;

In re Appln. of Shanker GUPTA
Application No. 10/056,567

N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid;
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid; or
N-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid.

48. (Original) The method of claim 35, wherein the compound of formula (1) is D-mannitol *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronate.

49. (Original) The method of claim 47, wherein the compound of formula (3) is *N*-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid.

50. (Original) The method of claim 35, wherein the mixture further comprises a water-miscible solvent.

51. (Original) The method of claim 50, wherein the water-miscible solvent is an alcohol.

52. (Original) The method of claim 51, wherein the alcohol is *tert*-butanol.

53. (Previously Presented) The method of claim 35, wherein mannitol and the compound of formula (3) are present in at least a 1:1 ratio.

54. (Previously Presented) The method of claim 35, wherein mannitol and the compound of formula (3) are present in at least a 5:1 ratio.

55. (Original) A lyophilized cake comprising the compound of claim 17.

56. (Previously Presented) A composition comprising the compound of claim 1 and a pharmaceutically-acceptable carrier.

57. (Previously Presented) A composition comprising the compound of claim 8 and a pharmaceutically-acceptable carrier.

58. (Previously Presented) A composition comprising the compound of claim 12 and a pharmaceutically-acceptable carrier.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

59. (Previously Presented) A composition comprising the compound of claim 16 and a pharmaceutically-acceptable carrier.

60. (Previously Presented) A composition comprising the compound of claim 17 and a pharmaceutically-acceptable carrier.

61. (Previously Presented) A composition comprising the compound of claim 24 and a pharmaceutically-acceptable carrier.

62. (Previously Presented) A composition comprising the compound of claim 28 and a pharmaceutically-acceptable carrier.

63. (Previously Presented) A composition comprising the compound of claim 32 and a pharmaceutically-acceptable carrier.

64. (Previously Presented) A lyophilized cake comprising the compound of claim 24.

65. (Previously Presented) A lyophilized cake comprising the compound of claim 28.

66. (Previously Presented) A lyophilized cake comprising the compound of claim 32.

67. (Previously Presented) The method of claim 35 further comprising (c) reconstituting the lyophilized mixture with a pharmaceutically-acceptable carrier.

68. (Previously Presented) The method of claim 41 further comprising (c) reconstituting the lyophilized mixture with a pharmaceutically-acceptable carrier.

69. (Previously Presented) The method of claim 45 further comprising (c) reconstituting the lyophilized mixture with a pharmaceutically-acceptable carrier.

70. (Previously Presented) The method of claim 48 further comprising (c) reconstituting the lyophilized mixture with a pharmaceutically-acceptable carrier.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

71. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 35 and (ii) a pharmaceutically-acceptable carrier.

72. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 41 and (ii) a pharmaceutically-acceptable carrier.

73. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 45 and (ii) a pharmaceutically-acceptable carrier.

74. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 48 and (ii) a pharmaceutically-acceptable carrier.

75. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 35.

76. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 41.

77. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 45.

78. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 48.

79. (Currently Amended) The compound of claim ~~12~~ 11, wherein P is (2-pyrazine)carbonyl.

80. (Previously Presented) A composition comprising the compound of claim 79 and a pharmaceutically-acceptable carrier.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

81. (Currently Amended) The compound of claim 28 27, wherein P is (2-pyrazine)carbonyl.
82. (Previously Presented) A composition comprising the compound of claim 81 and a pharmaceutically-acceptable carrier.
83. (Previously Presented) A lyophilized cake comprising the compound of claim 81.
84. (Currently Amended) The method of claim 45 44, wherein P is (2-pyrazine)carbonyl.
85. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 84 and (ii) a pharmaceutically-acceptable carrier.
86. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 84.
87. (Previously Presented) The compound of claim 1, wherein P and R together form a cyclic moiety.
88. (Currently Amended) The compound of claim 87, wherein Z^1 and Z^2 together form a moiety derived from ~~mannitol~~ D-mannitol.
89. (Previously Presented) The compound of claim 88, wherein
A is zero;
R is hydrogen or C_1-C_8 alkyl;
 R^3 is C_1-C_6 alkyl; and
P is (2-pyrazine)carbonyl.
90. (Previously Presented) A composition comprising the compound of claim 87 and a pharmaceutically-acceptable carrier.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

91. (Previously Presented) A composition comprising the compound of claim 88 and a pharmaceutically-acceptable carrier.

92. (Previously Presented) A composition comprising the compound of claim 89 and a pharmaceutically-acceptable carrier.

93. (Previously Presented) The compound of claim 17, wherein P and R together form a cyclic moiety.

94. (Currently Amended) The compound of claim 93, wherein Z^1 and Z^2 together form a moiety derived from ~~mannitol~~ D-mannitol.

95. (Previously Presented) The compound of claim 94, wherein

A is zero;

R is hydrogen or C_1 - C_8 alkyl;

R^3 is C_1 - C_6 alkyl; and

P is (2-pyrazine)carbonyl.

96. (Previously Presented) A composition comprising the compound of claim 93 and a pharmaceutically-acceptable carrier.

97. (Previously Presented) A composition comprising the compound of claim 94 and a pharmaceutically-acceptable carrier.

98. (Previously Presented) A composition comprising the compound of claim 95 and a pharmaceutically-acceptable carrier.

99. (Previously Presented) A lyophilized cake comprising the compound of claim 93.

100. (Previously Presented) A lyophilized cake comprising the compound of claim 94.

101. (Previously Presented) A lyophilized cake comprising the compound of claim 95.

In re Appln. of Shanker GUPTA
Application No. 10/056,567

102. (Previously Presented) The method of claim 35, wherein P and R together form a cyclic moiety.

103. (Previously Presented) The method of claim 102, wherein

A is zero;

R is hydrogen or C₁-C₈ alkyl;

R³ is C₁-C₆ alkyl; and

P is (2-pyrazine)carbonyl.

104. (Previously Presented) The method of claim 102 further comprising (c) reconstituting the lyophilized mixture with a pharmaceutically-acceptable carrier.

105. (Previously Presented) The method of claim 103 further comprising (c) reconstituting the lyophilized mixture with a pharmaceutically-acceptable carrier.

106. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 102 and (ii) a pharmaceutically-acceptable carrier.

107. (Previously Presented) A composition comprising (i) the compound of formula (1) prepared in accordance with the method of claim 103 and (ii) a pharmaceutically-acceptable carrier.

108. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 102.

109. (Previously Presented) A lyophilized cake comprising the compound of formula (1) prepared in accordance with the method of claim 103.